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| 10/551,292 | 09/28/2005 | Isabel Rego Santos | 1660 WO/US | 1556 |
| 7590 | | 07/01/2009 | | |
| Jeffrey S Boone | | | | |
| Mallinckrodt Inc | | | | |
| 675 McDonnell Boulevard | | | | |
| PO Box 5840 | | | | |
| St Louis, MO 63134 | | | | |
| | | | EXAMINER | |
| | | | SCHLIENTZ, LEAH H | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1618 | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/551,292

Applicant(s)

SANTOS ET AL.

Examiner

Leah Schlientz

Art Unit

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 April 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 11-13, 17, 25, 36, 38 and 41-52 is/are pending in the application.
- 4a) Of the above claim(s) 4, 5, 8, 11, 13, 17 and 25 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 36, 38, 43-49, 51 and 52 is/are allowed.
- 6) ☒ Claim(s) 1-3, 6, 7, 12, 41, 42 and 50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 September 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Examiner's Patent Drawing Review (PTO-946)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 4/20/2009, in reply to the Office Action mailed 1/23/2009, is acknowledged and has been entered. Claims 1,12 and 50 have been amended. Claims 1-8, 11-13, 17, 25, 36, 38 and 41-52 are pending, of which claims 4, 5, 8, 11, 13, 17 and 25 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claims 1-3, 6, 7, 12, 36, 38 and 41-52 are readable upon the elected invention and are examined herein on the merits for patentability.

Response to Arguments

Applicant's arguments have been fully considered but are moot in view of new grounds of rejection, set forth hereinbelow. Any rejection not reiterated herein has been withdrawn as being overcome by amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

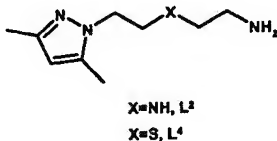
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 6, 7, 12, 41, 42 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alves *et al.* (*J. Chem. Soc. Dalton Trans*, 2002, p. 4714-4719) in view of Alberto (WO 00/50086).

Alves discloses the rhenium and ^{99m}technetium coordination capabilities of pyrazolyl containing ligands, such as pz*(CH₂)₂NH(CH₂)₂NH₂ (L²) and pz*(CH₂)₂S(CH₂)₂NH₂ (L⁴), where (pz* = 3,5 Me₂Pz), as shown below.

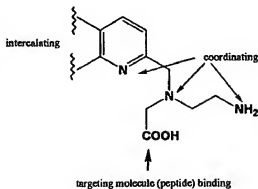


Such compounds are useful in the development of receptor-specific targeting molecules for use in nuclear medicine. The ligands presented in the study of Alves were presented as a part of research to access a general labeling protocol for biomolecules, namely peptides (page 4714, left column). The ligands are shown to

present a range of features, namely stability, solubility, coordination possibilities and **easy functionalization through** the pyrazolyl, the **amine groups** and the methylenic backbone, which make them promising for biomedical applications, **specifically for labeling peptides with the *fac*-[M(CO)₃]⁺ moiety** (page 4714, right column).

Accordingly, Alves discloses compounds meeting the formula as claimed in claim 1, but teaches a hydrogen at position R4, rather than a (CH₂)_n(COOH) group. Alves teaches that the ligands may be derivatized to carry a biomolecule (i.e. via functionalization at the amines). Alves does not specifically teach that such functionalization is achieved via a (CH₂)_n(COOH) group.

However, derivatization of an alkylamine moiety of a chelator via a carboxylate functional group is well-known in the art to be a method by which ^{99m}Tc chelating moieties may be conjugated to a biomolecule. See Alberto Abstract and page 11. For example, Alberto teaches compounds of the following formula:



The compounds of Alberto differ from the claims by the presence or pyridine rather than pyrazolyl ring.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to derivatize the amine (X, NH) of the ligands taught by Alves to carry a CH_2COOH group. One would have been motivated to do so because Alves teaches that said ligands are intended for the stabilization of the $[\text{M}(\text{CO})_3]^+$ core and for linking to biomolecules, and because Alves specifically teaches that said ligands offer easy functionalization through the amine (see Alves page 1474). Although Alves does not specifically teach that such functionalization occurs via a CH_2COOH group, it would have been obvious to one of ordinary skill in the art to utilize such groups because Alberto teaches that carboxyl groups on a short chain carbon moiety are groups which are typically used to link a biomolecule, such as an peptide, to an alkylamine moiety of a radionuclide chelator. One would have expected a reasonable degree of success in doing so because Alberto teaches that the use of such linking moieties is well-known and has been conventionally used in conjugating peptides (see abstract, page 11). Regarding claim 6, wherein n of the the $(\text{CH}_2)_n\text{COOH}$ is 2, such species are considered to be a homologues of CH_2COOH , it is considered that one of ordinary skill in the art would have found it obvious to provide the methyl or ethyl group homologues with the expectation of providing similar properties. See *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

Conclusion

Claims 36, 38, 43-49, 51 and 52 are allowed. Claims 1-3, 6, 7, 12, 41, 42 and 50 stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS